

REMARKS

The status of the claims is as follows:

Original: 11

Currently amended: 9, 10, 11, 13, 14 and 18

Previously presented: 12, 15-17, 19 and 20

Canceled: 1-8 and 21-25

Withdrawn: None

New: None

Claims 9-20 will be pending with entry of this amendment. Reconsideration is requested.

Amendments

Claims 21-25 have been canceled. Claims 1-8 were canceled in an earlier amendment.

In claim 9 R<sup>2</sup> and R<sup>4</sup> have been limited to H, and the option of R<sup>3</sup> and R<sup>3a</sup> being taken together with any intervening atoms to form a carbocyclic or heterocyclic ring has been removed.

Claims 10, 13 and 14 have been amended to conform to claim 9 as amended.

In claims 11 and 18, the word "and" has been inserted to make the recitation more clear.

The cancellations and amendments to the claims are without prejudice; i.e., Applicants reserve the right to pursue any canceled or deleted subject matter in one or more continuing applications.

None of the foregoing amendments introduces new matter.

Information Disclosure Statement

An information disclosure statement accompanies this amendment. The IDS cites Schmidt et al., Antimicrobial Agents and Chemotherapy 1978, vol. 14, pp. 672-679. The article describes the antimalarial activity of WR-194,965, an  $\alpha$ -amino-*o*-cresol derivative.

First Rejection under 35 U.S.C. § 103

Claims 9-25 have been rejected as being unpatentable over Burckhalter. Claims 21-25 have been canceled rendering the rejection moot as applied thereto. The rejection is traversed with respect to claims 9-20 as amended herein.

The claims as amended herein are directed to a method for the treatment of malaria comprising the administration of a compound of formula I. The compound of formula I is a 2-aminoalkyl phenol in which the amino moiety is NH<sub>2</sub>. By contrast, Burckhalter directs the person of

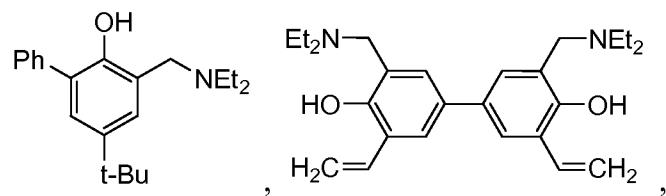
ordinary skill in the art toward 2-aminoalkylphenols in which the amino moiety is a secondary or tertiary amino; i.e., Burckhalter teaches antimarial compounds having the general formula at the top of the right column of page 1894, wherein the aminoalkyl group in the 2-position is  $-\text{CH}_2\text{NR}_1\text{R}_2$  where  $\text{R}_1$  is H or alkyl and  $\text{R}_2$  is alkyl. Consistent with the general formula on page 1894, only 1 of the 128 compounds disclosed in Burckhalter has a primary amine; i.e., 4-phenyl- $\alpha$ -amino-*o*-cresol which is the first entry in Table III (Compound III-1).

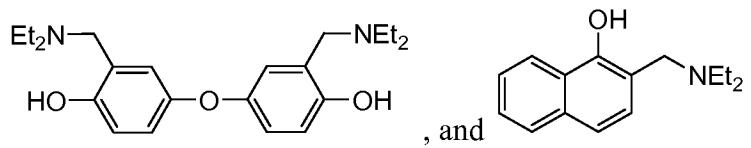
Furthermore, the compound of formula I in the claimed malaria treatment method is required to have substitution at both the 3- and 5-positions of the phenol ring and no substitution in the 4- and 6-positions. In contrast, as previously discussed in the amendment filed September 15, 2008, Burckhalter directs the person of ordinary skill in the art toward 2-aminoalkylphenols with substituents in the 4- and/or 6-positions. Nearly all of the substituted aminoalkylphenols disclosed in Burckhalter have a non-hydrogen substituent in the 4-position or in the 6-position or in both the 4- and 6-positions of the phenol ring. As one example, of the 34  $\alpha$ -amino-*o*-cresols listed in Table II (p.1897), 2 have no substitution on the phenol ring; 4 have a substituent in the 6-position; 9 have a substituent in the 4-position; 11 have 4,6-substitution; 5 have 4,5-substitution; 1 has 3,4,6-substitution; 1 has 3,5,6-substitution; and only one has 3,5-substitution. Burckhalter states (p. 1899, 2<sup>nd</sup> column under "Pharmacological Results") that of the compounds in Table II, the compound that "proved to be most effective" was Compound II-31 which is a compound with 4,6-substitution; i.e., 4-tert-butyl-6-cyclohexyl-2-[(diethylamino)methyl]phenol.

As another example, of the 28 aryl  $\alpha$ -amino-*o*-cresols listed in Table III, 1 has 5-substitution on the phenol ring; 6 have 4-substitution; 4 have 6-substitution; 1 has 2,3-substitution; 1 has 4,5-substitution; and 15 have 4,6-substitution. All but one of the Table III compounds have substitution in either or both the 4- and 6-positions. None of the Table III compounds has 3,5-substitution.

As still other examples, all 7 of the benzyl-type  $\alpha$ -diethylamino-*o*-cresols in Table IV have 4-substitution, 6-substitution or 4,6-substitution on the phenol ring; and all of the  $\alpha$ -diethylamino-*o*-cresols in Table V have 4-substitution. None has 3,5-substitution.

Furthermore, of the 128 compounds disclosed in the reference, the compounds which Burckhalter characterizes as "representative of some of the most interesting types thus far prepared in this particular group" (p. 1901 under the "Summary") are:





Three of these four compounds have substituents in either or both the 4- and 6-positions on the phenol ring, and the other compound is a naphthol which is even further removed from the instantly claimed invention.

Of the very few compounds disclosed in Burckhalter having substituents in the 3- and 5-positions, the closest is 2-[(diethylamino)methyl]-3,5-dimethylphenol (Compound II-24), which lies outside the scope of the instant method claims; i.e., the only alkyl substituent permitted in the 3- and 5-positions of the compounds employed in the instant invention is tert-butyl (vs. methyl in II-24) and the alkylamino substituent in the 2-position must be have an NH<sub>2</sub> moiety (vs. NEt<sub>2</sub> in II-24).

As mentioned above, Compound III-1 is the only compound in Burckhalter with a primary aminoalkyl in the 2-position. Compound III-1 is outside the scope of the claimed method; i.e., the compounds employed in the instant invention require substituents in both the 3- and 5-positions and no substitution in the 4- and 6-positions, whereas III-1 has a phenyl substituent in the 4-position and no substituents in the 3- and 5-positions.

Summarizing, Burckhalter directs the person of ordinary skill in the art toward aminoalkylphenols having a secondary or tertiary aminoalkyl in the 2-position and substitution in the 4- and/or 6-positions. This teaches away from the instant claims which employ compounds characterized by a 2-primary aminoalkyl group, substitution in both the 3- and 5-positions, and no substitution in the 4- and 6-positions. Withdrawal of this rejection is accordingly requested.

Second Rejection under 35 U.S.C. § 103

Claims 21 and 22 have been rejected as being unpatentable over Cragoe. Claims 21 and 22 have been canceled rendering this rejection moot. Withdrawal of the rejection is requested.

The application is believed to be in condition for allowance and passage to issue is requested.  
The Examiner is invited to telephone the undersigned should any minor matters need to be resolved before a Notice of Allowance can be mailed.

Respectfully submitted,

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